REMARKS

Claims 1-92 are pending, claims 1-83 and 91-92 are provisionally withdrawn from consideration and claims 84-90 are amended. The subject matter of claims 84-90 has been amended to clarify what the R^9 and R^{10} groups can separately be. Original claim 86 had specified that R^9 and R^{10} groups can separately be -NH-(C=O)-CH_2-halide, amine, maleimide, -N=C=O, -N=C=S, acyl halide, succinimidyl ester, sulfosuccinimidyl ester, sulfonyl halide, sulfonyl azide, alcohol, thiol, semicarbazide, hydrazine or hydroxylamine. The amendment to claim 86 indicates that R^9 and R^{10} groups can separately be, among other things, an alkyl chain derivatized with such groups, as supported by the description of R^9 and R^{10} in claim 84. Similarly, original claim 85 specified that R^9 and R^{10} groups can separately be sulfonate, amide or ether. Amended claim 85 indicates that R^9 and R^{10} groups can separately be, among other things, an alkyl chain derivatized with such groups, as supported by the description of R^9 and R^{10} in claim 84. Such description of the R^9 and R^{10} groups is supported throughout the specification and claims, for example, in claim 84 ("alkyl chain derivatized with charged groups"), in claim 85 and 86 as described above, in claim 88 where one R^9 is hydrogen, in the specification at Page 21, Lines 3-26, and in the structures at Pages 22-24. The amendment of claims 84-90 does not limit the scope of equivalents to which any claim element is entitled. Applicant submits that no new matter has been added by such amendment.

Applicant has carefully reviewed and considered the Restriction Requirement mailed on July 7, 2003, and traverses this Requirement as follows.

I. Claims 1-5, drawn to a compound of formula (I), comprising one or more aminooxy groups, classified in class 564, subclass 300.

II. Claims 6-7, drawn to a peptide comprising a backbone and one or more aminooxy groups, classified in class 514, subclass 2, and class 564, subclass 300.

III. Claims 8-43 and 61-66, drawn to a peptide conjugate of formula (III) or (IV), comprising a peptide or antibody as R^6 group, and a functional molecule D; a method for preparing a peptide conjugate comprising a peptide linked to a functional molecule; and a polypeptide biosensor, classified in class 514, subclass 2, class 564, subclass 300, and 424, subclass 179.1.

IV. Claims 44-48, drawn to a method of identifying an optimal position for placement of a functional molecule on a peptide having a peptide backbone and a known activity, wherein the functional group location does not substantially interfere with the known activity of the peptide; classified in class 514, subclass 2, and class 564, subclass 300.

V. Claims 49-60, drawn to a method of identifying an optimal position for placement of an environmentally-sensitive functional molecule on a peptide biosensor having a peptide backbone, wherein the functional group location provides the strongest signal change in response to an environmental change, classified in class 514, subclass 2, and class 564, subclass 300.

VI. Claims 67-69, drawn to a fusion protein comprising Rho GtPase protein domain linked to a fluorescent protein via a peptide conjugate, classified in class 435, subclass 69.7.

VII. Claims 70-72, drawn to a nucleic acid encoding a fusion protein comprising Rho GTPase protein domain linked to a fluorescent protein via a peptide conjugate; an expression vector comprising the nucleic acid; or a cell comprising the vector, classified in class 536, subclass 23.5, and class 435, subclasses 320.1 and 325.

VIII. Claims 73-75, drawn to a method of detecting GTP activation of Rho GTPase protein in a cell using a polypeptide biosensor containing a fluorescent dye, which can undergo fluorescence resonance energy transfer with a fluorescent dye on the GTP activated Rho GTPase protein; classified in class 514, subclass 2, and class 564, subclass 300.

IX. Claims 76 and 78-81, drawn to a method of detecting GTP activation of a Rho GTPase protein by contacting a polypeptide biosensor with a test substance, wherein the polypeptide is operatively linked to an environmentally sensitive dye, which will emit a signal of a different lifetime, intensity or wavelength when the polypeptide biosensor is bound to the GTP activated Rho GTPase protein as to the polypeptide biosensor is not bound; classified in class 514, subclass 2, and class 564, subclass 300.

X. Claims 77 and 78-81, drawn to a method of detecting GTP activation of a Rho GTPase protein in a cell using a polypeptide biosensor, wherein the polypeptide is operatively linked to an environmentally sensitive dye, which will emit a signal of a different lifetime, intensity or wavelength when the polypeptide biosensor is bound to the GTP

activated Rho GTPase protein as to the polypeptide biosensor is not bound; classified in class 514, subclass 2, and class 564, subclass 300.

XI. Claim 82, drawn to a method of detecting binding of an antibody to an antigen which comprises reacting an antibody comprising a peptide conjugate with an antigen and detecting an antibody-antigen complex; classified in class 435, subclass 7.1.

XII. Claim 83, drawn to a method of detecting binding of an antigen to an antibody which comprises reacting an antigen comprising a peptide conjugate with an antibody and detecting an antibody-antigen complex; classified in class 435, subclass 7.1.

XIII. Claims 84-90, drawn to a fluorescent compound comprising heterocyclic rings, classified in class 548, subclass 100 and 122.

XIV. Claims 91 and 92, drawn to a biological molecule linked to the fluorescent compound of claim 84, classified in class 548, subclass 100; class 514, subclass 2; class 424, subclass 179.1, and class 536, subclass 23.1.

Applicant provisionally elects, with traverse, the claims of Group XIII (claims 84-90). Applicant also provisionally elects, with traverse, functional groups $C(CH_3)_2$ for R^8, hydrogen for R^9, alkyl-SO_3 for R^{10}, C=O for R^{11}, and SO_2 for R^{12}. Applicant hereby provisionally withdraws the claims of Group I-XII and XIX (claims 1-83 and 91-92) without prejudice, reserving the right to refile them in a continuation or divisional application.

The Restriction Requirement is traversed on the basis that Restriction Requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of an entire application can made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. It is respectfully submitted that the search and examination, for example, of the claims of Groups I – V, VIII, IX, and X, having related subject matter classified in class 564, subclass 300 and class 514, subclass 2, can be made without serious burden on the Office. Given the close relationship between the subject matter of the claims in these groups, no additional serious burden results from the search and examination of the claims within these Groups, claims 1-66 and 73-81. Similarly, it is respectfully submitted that the search and examination, for example, of the claims

of Groups XI and XII, having related subject matter classified in class 435, subclass 7.1, can be made without serious burden on the Office. Given the close relationship between the subject matter of the claims in these groups, no additional serious burden results from the search and examination of the claims within these Groups, claims 82-83. In addition, It is respectfully submitted that the search and examination, for example, of the claims of Groups XIII and XIV, having related subject matter classified in class 548, subclass 100, can be made without serious burden on the Office. Given the close relationship between the subject matter of the claims in these groups, no additional serious burden results from the search and examination of the claims within these Groups, claims 84-92. Thus, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

Applicants further traverse the requirement for electing a single functional group for each of R^8, R^9, R^{10}, R^{11}, and R^{12}. As provided by the MPEP, species may be related inventions and need not be subject to restriction. *See* MPEP § 806.04(b). In particular, where species are claimed under a common genus and are related, the question of restriction is determined by the practice applicable to election of species and the practice applicable to other types of restrictions. *See id.* Here, each of R^9 and $R^{10}$are claimed in one or more generic claims and those generic claims explicitly define how those sequences are related (as charged or reactive groups as recited claim 84. Accordingly, the functional groups of R^9 and $R^{10}$are related and Applicants respectfully request that the Examiner reconsider whether restriction is proper in this case.

Applicants also respectfully remind the Examiner that they are entitled to examination of a reasonable number of species and election of species is for the convenience of the Examiner in initiating the search.. Here each of R^8, R^{11} and R^{12} are separately selected from a small number of species: CO, SO_2, $C{=}C(CN)_2$, S, O or $C(CH_3)_2$. Hence, this is a reasonable number of species and examination thereof would not constitute a burden.

Therefore, withdrawal or modification of this Requirement is appropriate and is respectfully requested.

A favorable examination of the merits of this patent application is respectfully requested. The Examiner is invited to telephone Applicant's attorney (516-795-6820) to facilitate prosecution of this application. Please charge any additional fees deemed necessary to Deposit Account 19-0743.

Respectfully submitted,

KLAUS M. HAHN ET AL.

By their Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 373-6939

Date Oct. 7, 2003 By Robin A. Chadwick

Robin A. Chadwick
Reg. No. 36,477

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 7th day of October, 2003.

Candis B. Buending
Name

Candis B. Buending
Signature